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INTROL® CF Panel I Control v.02

INTENDED USE:

INTROL® CF Panel I Control v.02 is intended for *in vitro* diagnostic use as a quality control to monitor analytical performance of the extraction, amplification and detection steps of diagnostic assays used in the detection of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene mutations and variants. This product is intended to be extracted and analyzed routinely with each CFTR assay run.

The INTROL CF Panel I Control v.02 is designed to monitor the detection of 38 CFTR mutations associated with cystic fibrosis, including the 23 mutations recommended for testing by American College of Medical Genetics (ACMG) and American College of Obstetricians and Gynecologists (ACOG). The INTROL CF Panel I Control also monitors 3 polymorphisms (I506V, I507V, F508C) and the 5/7/9T variants.

PRODUCT DESCRIPTION:

INTROL CF Panel I Control v.02 consists of synthetic CFTR DNA suspended in a matrix of carrier DNA of non-human species, preservatives, dye, and stabilizers. The synthetic DNA contains all 27 CFTR gene exons plus intronic borders, and contains specific mutations and polymorphisms which are divided among 3 bottles. The specific mutations present in each bottle are listed in Table 1; all other CFTR sequence is wild type. CFTR mutations that are not listed cannot be detected in the INTROL CF Panel I Control v.02.

CFTR DNA is stabilized in the matrix and released when processed through common extraction methods as if it were a whole blood specimen. Following extraction, the released DNA can be used in common amplification based molecular assays techniques. Because INTROL CF Panel I Control v.02 is designed to mimic the whole blood sample, the resulting copy number of the artificial CFTR segment, after extraction, will be similar to that found in a processed human whole blood sample (v/v).

INSTRUCTIONS FOR USE:

Extract and analyze INTROL CF Panel I Control v.02 as you would a whole blood specimen:

1. Allow INTROL CF Panel I Control v.02 to reach room temperature (18° – 25°C).
2. Thoroughly mix the controls prior to opening by inverting the bottle several times immediately before use, or by placing on an automated mixer.
3. Extract INTROL CF Panel I Control v.02 in the same manner as a whole blood clinical specimen. Use the same volume of INTROL CF Panel I Control v.02 that would be used for a patient sample in your lab.
   Note 1: Certain extraction methods may require additional processing of control material, such as dilution prior to analysis.
   Note 2: The level of CFTR DNA present in the extracted control may not be detectable with certain quantitation methods and is not quantifiable by spectrophotometer measurements.
4. Analyze the extracted DNA as you would genomic DNA. If dilutions or other preparations of the extracted DNA are required as part of the testing procedure, handle the INTROL CF Panel I Control v.02 DNA according to your standard laboratory protocol.
5. Tightly recap each bottle after use and store refrigerated (2° – 8°C).
6. Controls should be tested routinely as a matter of Good Laboratory Practice and according to guidelines or requirements of local, state, and/or federal regulations or accrediting organizations. The frequency of running the control material will depend on individual laboratory practice and may vary according to the analytical system being used.

STORAGE:

Upon receipt and after opening, the material should be stored at 2° – 8°C. Do not freeze.

STABILITY:

Unopened INTROL CF Panel I Control v.02 material is stable through the expiration date printed on each bottle when stored refrigerated (2° – 8°C). Opened material returned to the refrigerator (2° – 8°C) shortly after use is stable for thirty (30) days from the date of opening. Contact MMQCI if control material was inadvertently frozen or exposed to high temperatures.

Table 1. Composition of INTROL CF Panel I Control v.02 includes the following combinations of CFTR mutations and polymorphisms (plus wild type sequence covering 27 CFTR exons). Polymorphisms are in parentheses ( ).

Allele	Genotype
G106a or G106a-1	
7T*	7T / 7T
(I507V)*	I507V / WT
(F508C)*	F508C / WT
S549N/ S549R	Heterozygous
S1251N	Heterozygous
G106b or G106b-1	
E60X	Homozygous mutant
G85E*	Homozygous mutant
I148T	Homozygous mutant
621+1G>T*	Homozygous mutant
711+1G>T*	Homozygous mutant
1078delT	Homozygous mutant
R334W*	Homozygous mutant
R347P*	Homozygous mutant
9T*	9T / 9T
A455E*	Homozygous mutant
del F508*	Homozygous mutant
V520F	Homozygous mutant
1717-1G>A*	Homozygous mutant
G542X*	Homozygous mutant
G551D*	Homozygous mutant
2184delA*	Homozygous mutant
2789+5G>A*	Homozygous mutant
3120+1G>A*	Homozygous mutant
3199del6	Homozygous mutant
D1152H	Homozygous mutant
R1162X*	Homozygous mutant
3659delC*	Homozygous mutant
3849+10kbC>T*	Homozygous mutant
3876delA	Homozygous mutant
3905insT	Homozygous mutant
W1282X*	Homozygous mutant
N1303K*	Homozygous mutant
G106c or G106c-1	
394delTT	Heterozygous
R117H*	Heterozygous
R347H	Heterozygous
5T* / 7T*	Heterozygous
(I506V)*	I506V / WT
del I507*	Heterozygous
R553X*	Heterozygous
2183AA>G	Heterozygous

*ACMG / ACOG Panel

PRECAUTIONS AND WARNINGS:

- This product contains 23% ethanol (v/v) and could be flammable. Keep away from open flames.
- This product does not contain any biological material of human origin.
- The laboratory should follow Good Laboratory Practice (GLP) and establish its own performance characteristics for INTROL CF Panel I in demonstrating adequate system performance.
- MMQCI CF products are not intended to be frozen and are shipped with a DO NOT FREEZE label.

LIMITATIONS:

- Interferences and cross-reactions may occur with some detection methods and confound interpretation of the test. Please refer to the kit manufacturers package insert to review possible cross-reactions and near neighbor interferences identified in the method.
- Recoveries may vary depending on extraction method, instrumentation, cycle time / temperature, reagents, method variation, and systematic or random errors.

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G106 EN Issued: September 2025 Rev.01

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PERFORMANCE CHARACTERISTICS:
All INTROL CF Panel I Control v.02 products are tested by an FDA-cleared CFTR mutation detection method before being released for market distribution. Any mutations not tested by the FDA-cleared method are sequenced bidirectionally before product is released. All mutations must be detected.

Clinical Evaluation – External Sites:
The clinical study performed at the external sites evaluated reproducibility of INTROL CF Panel I Control material with respect to within run, between run, between sites, between lots, and between methods.

Evaluation using different extraction methods:

# extraction methods	21
# laboratories	134
# successful laboratory extractions	129
percent successful	96% *

*Five laboratories didn't continue after DNA extraction because DNA quantitation method they used indicated that no DNA was extracted/isolated. Considering that the level of synthetic CFTR DNA present in the extracted control may not be detectable with certain quantitation methods, there is a possibility that extractions in these 5 laboratories may have been successful; however, this could not be assessed because the assays were not performed.

INTROL CF Panel I Control v.02 material has been tested using CFTR assays at 10 external sites, 8 of which were clinical laboratories representing intended user. Samples from 11 different manufacturing lots were tested at minimally 3 external sites in at least 3 separate runs. Results are summarized in Table 2.

Table 2. External site evaluations.

Method	Site	# of Lots	# of Runs	Total Calls	% Correct Calls
Tag-It™	1	10	9	223	100%
	2	3	9	138	100%
	3	1	1	6	100%
	4	1	1	7	100%
	5	1	1	4	100%
eSensor ®	6	5	1	30	100%
Other Amplification methods	7	5	1	38	100%
	8	3	1	31	100%
	9	1	2	7	100%
	10	5	40	649	100%
6 methods		**11 Lots[1]**	**66 Runs**	**1133 Calls**	**100% Correct**

1. Each bottle is processed independently and has its own lot number.

Expected Results:
Expected results with the INTROL CF Panel I Control v.02 using an FDA-cleared CFTR assay are presented in Table 3.

Table 3. Results with the INTROL CF Panel I Control v.02 using an FDA cleared CFTR assay.

Method	Correctly Identified Alleles	No Call or Other	Not Tested by Assay
Tag-It™	All wt alleles 7T, I507V, F508C, S549R, G85E, I148T, 621+1G>T, 711+1G>T, 1078delT, R334W, R347P, 9T, A455E, delF508, V520F, 1717+1G>A, G542X, G551D, R560T, 1898+1G>A, 2184delA, 2789+5G>A, 3120+1G>A, R1162X, 3659delC, 3849+10kbC>T, 3876delA, 3905insT, W1282X, N1303K, 394delTT, R117H, R347H, 5T/7T, I506, delI507, R553X, 2183AA>G	S549N: MUT[1]	S1251N, E60X, 2143delT 3199del6, D1152H,

1 Detected as homozygous mutant.

ORDERING INFORMATION:
INTROL® Cystic Fibrosis Panel I Control v.02

Part Number: G106ac
CONT Kit Contains: 3 bottles x 2mL
1 each G106a, G106b, and G106c

Part Number: G106ac-1
CONT Kit Contains: 3 bottles x 1mL
1 each G106a-1, G106b-1, and G106c-1

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G106 EN Issued: September 2025 Rev.01